Dynamic regulation of mRNA decay during neural development.

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Public Summary:
BACKGROUND: Gene expression patterns are determined by rates of mRNA transcription and decay. While transcription is known to regulate many developmental processes, the role of mRNA decay is less extensively defined. A critical step toward defining the role of mRNA decay in neural development is to measure genome-wide mRNA decay rates in neural tissue. Such information should reveal the degree to which mRNA decay contributes to differential gene expression and provide a foundation for identifying regulatory mechanisms that affect neural mRNA decay. RESULTS: We developed a technique that allows genome-wide mRNA decay measurements in intact Drosophila embryos, across all tissues and specifically in the nervous system. Our approach revealed neural-specific decay kinetics, including stabilization of transcripts encoding regulators of axonogenesis and destabilization of transcripts encoding ribosomal proteins and histones. We also identified correlations between mRNA stability and physiologic properties of mRNAs; mRNAs that are predicted to be translated within axon growth cones or dendrites have long half-lives while mRNAs encoding transcription factors that regulate neurogenesis have short half-lives. A search for candidate cis-regulatory elements identified enrichment of the Pumilio recognition element (PRE) in mRNAs encoding regulators of neurogenesis. We found that decreased expression of the RNA-binding protein Pumilio stabilized predicted neural mRNA targets and that a PRE is necessary to trigger reporter-transcript decay in the nervous system. CONCLUSIONS: We found that differential mRNA decay contributes to the relative abundance of transcripts involved in cell-fate decisions, axonogenesis, and other critical events during Drosophila neural development. Neural-specific decay kinetics and the functional specificity of mRNA decay suggest the existence of a dynamic neurodevelopmental mRNA decay network. We found that Pumilio is one component of this network, revealing a novel function for this RNA-binding protein.

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